REMARKS

The claims have been amended to clarify the invention and to distinguish explicitly the cited art (although the distinction was, applicants believe, present in the claims previously). The critical feature, that the biologically active agent be contained in the lipids/surfactant layer, was already present in the claims, but has been more clearly stated. Claim 71 has been amended to note that the particles have a fluorocarbon core and that the coated nanoparticles are coupled to a targeting ligand. Although applicants believe that "emulsion" is an appropriate word in this context, in order to expedite prosecution, it has been replaced with "composition."

For completeness, claims 87-93 have also been added, which list specific drugs that are to be included in the layer. These are supported on page 18, line 21 to page 20, line 21. No new matter has been added, and entry of the amendment is respectfully requested.

The Invention

The invention resides in the discovery that by immobilizing the lipid/surfactant coated particles of the invention at a target and prolonging the interaction of the lipid/surface layer with the target, enhanced drug delivery can be accomplished when the drug resides in this layer. Applicants are unable to find this suggestion in the cited prior art.

The Rejection Under 35 U.S.C. § 112, paragraph 2

As suggested by the Office, claim 71 has been redrafted. As stated above, while applicants believe the word "emulsion" is appropriate, this word has been changed to "composition" to expedite prosecution. Claim 71 has also been amended to clarify that it is the coated particle to which the targeting ligand is attached. Presumably, the Office believed that because the claim

simply stated "particle," that the lipid/surfactant layer would block the targeting agent from coming into contact with the target. This is not the case; the targeting agent is available at the surface of the particle, and can often be attached through the lipid/surfactant layer specifically.

It is believed the amendments obviate this basis for rejection as it pertains to claim 71.

The word "mimetics" has been deleted from claim 75.

Double Patenting

Claims 71-86 were rejected as assertedly obvious over claims 30-60 of the parent case, which issued as U.S. Patent No. 6,676,963. A terminal disclaimer with respect to the '963 patent is submitted herewith.

The Art Rejections

Claims 71-86 were rejected as assertedly anticipated by patents issued to the inventors herein: 5,690,907; 5,780,010; and 5,958,371. It is believed that the requirement that the biologically active agent be within the layer containing the biologically active agent has been overlooked. No such requirement or suggestion is set forth in the three documents cited by the Office.

The only discussion of biologically active agents associated with the particles described in the cited art that applicants are able to find is in column 7 of the '907 patent, beginning at line 48. Similar passages are found in the '010 patent at column 7, beginning at line 60, and in the '371 patent, also in column 7, beginning at line 60. This description says merely that biologically active agents (including drugs) are "incorporated in the liquid encapsulated *particles* and become part of the conjugate bound to a specific biological surface for therapeutic action." There is no description

which requires that the drug be present in the lipid surfactant *layer*. There are no examples in these documents whereby a drug is associated with the particles; thus, there is no inherent anticipation by virtue of a preparation procedure. As each and every element of the claim is not set forth in the document, anticipation cannot be found.

This is particularly the case for claims 87-93, wherein specific pharmaceuticals not set forth in the cited documents are included in the lipid/surfactant layer. Accordingly, this basis for rejection may properly be withdrawn.

Claims 71 and 74-86 were rejected as assertedly obvious over WO 95/03829 in combination with Long (U.S. Patent No. 4,987,154). Respectfully, this combination does not suggest the invention as claimed. This is immediately apparent from the picture on the cover page of the '829 publication, which shows that the drug is embedded in the particle itself and not in a layer on its surface. Thus, more is lacking in the '829 application than simply the presence of a fluorocarbon. If a perfluorocarbon were simply substituted for the oil particle of the '829 patent, the presently claimed particles would not result, as there is no disclosure of any outer coating on the oil particles of '829. Thus, these documents, even if combined, would not suggest the invention.

It is noted that in the discussion of delivery of drugs using fluorocarbons in the '154 patent in column 12, lines 23-44, there is no suggestion of including the drug in a lipid/surfactant layer either; rather, presumably the drugs are included in the fluorocarbon itself. Thus, if '154 is combined with '829, the methods of the invention do not result – one would simply obtain a fluorocarbon in substitution for the oil, whereas in the present invention the drug must be present in the lipid/surfactant layer which coats the perfluorocarbon.

For this reason, the rejection under § 103 may also be withdrawn.

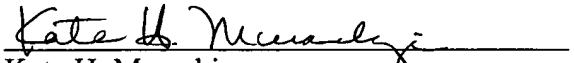
SUMMARY

The present claims require that the therapeutic agent to be delivered be in the lipid/surfactant layer coating fluorocarbon particles. Although fluorocarbon particles are discussed in the three Lanza patents cited as anticipatory, there is no teaching or suggestion that the drugs be delivered from the lipid/surfactant layer. This is a requirement of all claims. Further, the combination of WO 95/03829 with U.S. 4,987,154, even if made, does not suggest the invention as claimed. Rather, the combination would result in the drug being included in the fluorocarbon itself, not in the outer layer.

Accordingly, it is believed that all pending claims, claims 71-93, are in a position for allowance, and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 532512000401.

Respectfully submitted,

Dated: January 7, 2005 By: 

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